

CLAIMS

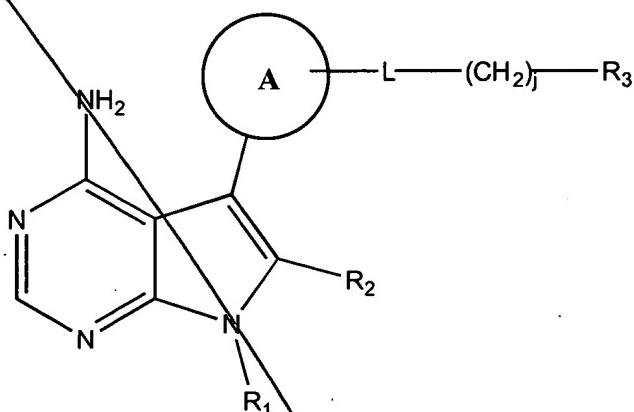
We claim:

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1. A compound represented by the following structural formula:

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and pharmaceutically acceptable salts thereof, wherein:

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Ring A is a six membered aromatic ring or a five or six membered heteroaromatic ring which is optionally substituted with one or more substituents selected from the group consisting of a substituted or unsubstituted aliphatic group, a halogen, a substituted or unsubstituted aromatic group, substituted or unsubstituted heteroaromatic group, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, cyano, nitro, -NR₄R₅, -C(O)₂H, -OH, a substituted or unsubstituted alkoxy carbonyl, -C(O)₂-haloalkyl, a substituted or unsubstituted alkylthio ether, a substituted or unsubstituted alkylsulfoxide, a substituted or unsubstituted alkylsulfone, a substituted or unsubstituted arylthio ether, a substituted or unsubstituted arylsulfoxide, a substituted or unsubstituted arylsulfone, a substituted or unsubstituted alkyl carbonyl, -C(O)-haloalkyl, a substituted or unsubstituted

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aliphatic ether, a substituted or unsubstituted aromatic ether, a substituted or unsubstituted carboxamido, tetrazolyl, trifluoromethylsulphonamido, trifluoromethylcarbonylamino, a substituted or unsubstituted alkynyl, a substituted or unsubstituted alkyl amido or alkylcarboxamido; a substituted or unsubstituted aryl amido or arylcarboxamido, a substituted or unsubstituted styryl and a substituted or unsubstituted aralkyl amido or aralkylcarboxamido;

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L is -O-; -S-; -S(O)-; -S(O)₂-; -N(R)-; -N(C(O)OR)-; -N(C(O)R)-; -N(SO₂R)-; -CH₂O-; -CH₂S-; -CH₂N(R)-; -CH(NR)-; -CH₂N(C(O)R))-; -CH₂N(C(O)OR)-; -CH₂N(SO₂R)-; -CH(NHR)-; -CH(NHC(O)R)-; -CH(NHSO₂R)-; -CH(NHC(O)OR)-; -CH(OC(O)R)-; -CH(OC(O)NHR)-; -CH=CH-; -C(=NOR)-; -C(O)-; -CH(OR)-; -C(O)N(R)-; -N(R)C(O)-; -N(R)S(O)-; -N(R)S(O)₂-; -OC(O)N(R)-; -N(R)C(O)N(R)-; -NRC(O)O-; -S(O)N(R)-; -S(O)₂N(R)-; -N(C(O)R)S(O)-; -N(C(O)R)S(O)₂-; -N(R)S(O)N(R)-; -N(R)S(O)₂N(R)-; -C(O)N(R)C(O)-; -S(O)N(R)C(O)-; -S(O)₂N(R)C(O)-; -OS(O)N(R)-; -OS(O)₂N(R)-; -N(R)S(O)O-; -N(R)S(O)₂O-; -N(R)S(O)C(O)-; -N(R)S(O)₂C(O)-; -SON(C(O)R)-; -SO₂N(C(O)R)-; -N(R)SON(R)-; -N(R)SO₂N(R)-; -C(O)O-; -N(R)P(OR')O-; -N(R)P(OR')-; -N(R)P(O)(OR')O-; -N(R)P(O)(OR')-; -N(C(O)R)P(OR')O-; -N(C(O)R)P(OR')-; -N(C(O)R)P(O)(OR')O- or -

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20 N(C(O)R)P(OR')-, wherein R and R' are each, independently, -H, an acyl group, a substituted or unsubstituted aliphatic group, a substituted or unsubstituted aromatic group, a substituted or unsubstituted heteroaromatic group, or a substituted or unsubstituted cycloalkyl group; or

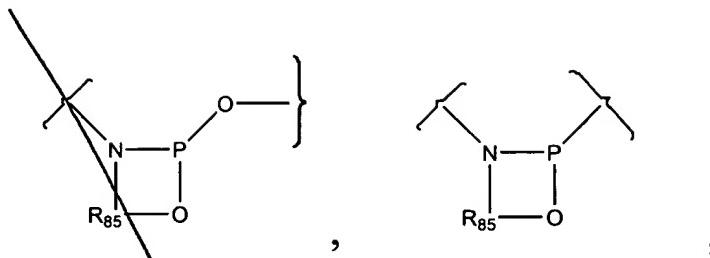
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L is -R_bN(R)S(O)₂-; -R_bN(R)P(O)-, or -R_bN(R)P(O)O-, wherein R_b is an alkylene group which when taken together with the sulphonamide, phosphinamide, or phosphonamide group to which it is bound forms a five or six membered ring fused to ring A; or

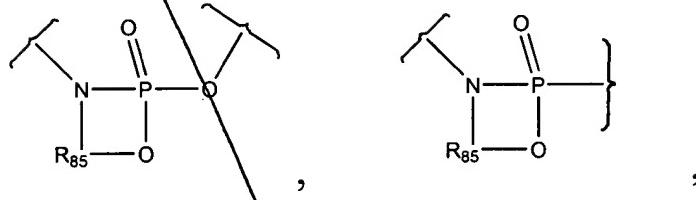
L is represented by one of the following structural formulas:

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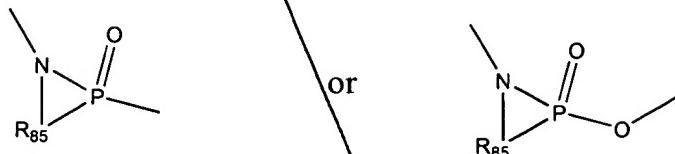
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wherein R₈₅ taken together with the phosphinamide, or phosphonamide is a 5-, 6-, or 7-membered, aromatic, heteroaromatic or heterocycloalkyl ring system;

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R₁ is -H, 2-phenyl-1,3-dioxan-5-yl, a C1-C6 alkyl group, a C3-C8 cycloalkyl group, a C5-C7 cycloalkenyl group or an optionally substituted phen(C1-C6 alkyl) group, wherein the alkyl, cycloalkyl and cycloalkenyl groups are optionally substituted by one or more groups of formula -OR^a; provided that -OR^a is not located on the carbon attached to nitrogen;

R^a is -H or a C1-C6 alkyl group or a C3-C6 cycloalkyl;

B2
cont

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R_2 is -H, a substituted or unsubstituted aliphatic group, a substituted or unsubstituted cycloalkyl, a halogen, -OH, cyano, a substituted or unsubstituted aromatic group, a substituted or unsubstituted heteroaromatic group, a substituted or unsubstituted heterocycloalkyl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted heteroaralkyl, $-NR_4R_5$, or $-C(O)NR_4R_5$;

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R_3 is a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted aromatic group, a substituted or unsubstituted heteroaromatic group, or a substituted or unsubstituted heterocycloalkyl; or L is $NRSO_2^-$, $NRC(O)-$, $NRC(O)O-$, $-S(O)_2NR-$, $-C(O)NR-$ or $-OC(O)NR-$, and R_3 is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl or substituted or unsubstituted aralkyl;

provided that j is 0 when L is $-CH_2NR-$, $-C(O)NR-$ or $-NRC(O)-$ and R_3 is azacycloalkyl or azaheteroaryl; and

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provided that j is 0 when L is $-O-$ and R_3 is phenyl;

R_4 , R_5 and the nitrogen atom together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted heterobicycloalkyl or a substituted or unsubstituted heteroaromatic; or

R_4 and R_5 are each, independently, -H, azabicycloalkyl, a substituted or unsubstituted alkyl group or Y-Z;

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Y is selected from the group consisting of $-C(O)-$, $-(CH_2)_p-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $(CH_2)_pO-$, $-(CH_2)_pNH-$, $-(CH_2)_pS-$, $-(CH_2)_pS(O)-$, and $-(CH_2)_pS(O)_2-$;

p is an integer from 0 to 6;

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Z is a substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; and

j an integer from 0 to 6.

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2. The compound of Claim 1, wherein R₃ is selected from the group consisting of a substituted or unsubstituted phenyl, a substituted or unsubstituted naphthyl, a substituted or unsubstituted pyridyl, a substituted or unsubstituted thieryl, a substituted or unsubstituted benzotriazole, a substituted or unsubstituted tetrahydropyranly, a substituted or unsubstituted tetrahydrofuranly, a substituted or unsubstituted dioxane, a substituted or unsubstituted dioxolane, a substituted or unsubstituted quinoline, a substituted or unsubstituted thiazole, substituted or unsubstituted isoxazole, substituted or unsubstituted cyclopentanyl, a substituted or unsubstituted bezofuran, substituted or unsubstituted benzothiophene, substituted or unsubstituted benzisoxazole, substituted or unsubstituted benzothiazole, substituted or unsubstituted benzothiazole, substituted or unsubstituted bezoxazole, substituted or unsubstituted benzoxazole, substituted or unsubstituted bezimidazole, substituted or unsubstituted benzoxadiazole, substituted or unsubstituted benzothiadiazole, substituted or unsubstituted isoquinoline, substituted or unsubstituted quinoxaline, substituted or unsubstituted indole and substituted or unsubstituted pyrazole.

3. The compound of Claim 2 wherein R₃ is substituted with one or more substituent selected from the group consisting of F, Cl, Br, I, CH₃, NO₂, OCF₃, OCH₃, CN, CO₂CH₃, CF₃, t-butyl, pyridyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted benzyl, substituted or unsubstituted benzenesulfonyl, substituted or unsubstituted phenoxy, substituted or unsubstituted phenyl, substituted or unsubstituted amino, carboxyl, substituted or unsubstituted tetrazolyl, styryl, -S-(substituted or unsubstituted aryl), -S-(substituted or unsubstituted heteroaryl), substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocycloalkyl, alkynyl, -C(O)NR_fR_g, R_c and CH₂OR_c; R_f, R_g and the nitrogen atom together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted heterobicycloalkyl or a substituted or unsubstituted heteroaromatic
- S J C 2*

Su C2

R_f and R_g are each, independently, -H, a substituted or unsubstituted aliphatic group or a substituted or unsubstituted aromatic group; and

Su C2

5 R_e is hydrogen, or substituted or unsubstituted alkyl or substituted or unsubstituted aryl, $-W-(CH_2)_t-NR_dR_e$, $-W-(CH_2)_t-O\text{-alkyl}$, $-W-(CH_2)_t-S\text{-alkyl}$, $-W-(CH_2)_t-OH$;

t is an integer from 0 to 6;

W is a bond or $-O-$, $-S-$, $-S(O)-$, $-S(O)_2-$, or $-NR_k-$;

R_k is -H or alkyl; and

10 R_d , R_e and the nitrogen atom to which they are attached together form a 3, 4, 5, 6 or 7-membered substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heterobicyclic group; or

R_d and R_e are each, independently, -H, alkyl, alkanoyl or $-K\text{-}D$;

K is $-S(O)_2-$, $-C(O)-$, $-C(O)NH-$, $-C(O)_2-$, or a direct bond;

15 D is a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted heteroaromatic group, a substituted or unsubstituted heteroaralkyl, a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted heterocycloalkyl, a substituted or unsubstituted amino, a substituted or unsubstituted aminoalkyl, a substituted or unsubstituted aminocycloalkyl, $COOR_1$, or substituted or unsubstituted alkyl; and

20 R_i is a substituted or unsubstituted aliphatic group or a substituted or unsubstituted aromatic group.

Su C3

Rule 1.12b
rule 3.25

3. The compound of Claim 3, wherein R_3 is a substituted or unsubstituted phenyl threnyl, benzoxadiazolyl or benzothiadiazolyl.

Rule 1.12b
rule 5

4. The compound of Claim 1, wherein ring A is selected from the group consisting of a substituted or unsubstituted phenyl, a substituted or unsubstituted naphthyl, a substituted or unsubstituted pyridyl, and a substituted or unsubstituted indole.

Su C3

Rule 126

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5. The compound of Claim 5 wherein ring A is substituted with one or more substituent selected from the group consisting of F, Cl, Br, I, CH₃, NO₂, OCF₃, OCH₃, CN, CO₂CH₃, CF₃, t-butyl, pyridyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted benzyl, substituted or unsubstituted benzenesulfonyl, substituted or unsubstituted phenoxy, substituted or unsubstituted phenyl, substituted or unsubstituted amino, carboxyl, substituted or unsubstituted tetrazolyl, styryl, -S-(substituted or unsubstituted aryl), -S-(substituted or unsubstituted heteroaryl), substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocycloalkyl, alkynyl, -C(O)NR_fR_g, R_c and CH₂OR_c;

10 R_f, R_g and the nitrogen atom together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted heterobicycloalkyl or a substituted or unsubstituted heteroaromatic; or

15 R_f and R_g are each, independently, -H, a substituted or unsubstituted aliphatic group or a substituted or unsubstituted aromatic group; and

R_c is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, -W-(CH₂)_t-NR_dR_e, -W-(CH₂)_t-O-alkyl, , -W-(CH₂)_t-S-alkyl, or -W-(CH₂)_t-OH;

t is an integer from 0 to 6;

20 W is a bond or -O-, -S-, -S(O)-, -S(O)₂-, or -NR_k-;

R_k is -H or alkyl; and

R_d, R_e and the nitrogen atom to which they are attached together form a 3, 4, 5, 6 or 7-membered substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted heterobicycloalkyl or a substituted or unsubstituted heteroaromatic; or

25 R_d and R_e are each, independently, -H, alkyl, alkanoyl or -K-D;

K is -S(O)₂-, -C(O)-, -C(O)NH-, -C(O)₂-, or a direct bond;

D is a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted

5 heteroaromatic group, a substituted or unsubstituted heteroaralkyl, a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted heterocycloalkyl, a substituted or unsubstituted amino, a substituted or unsubstituted aminoalkyl, a substituted or unsubstituted aminocycloalkyl, COOR_i, or a substituted or unsubstituted alkyl; and

R_i is a substituted or unsubstituted aliphatic group or a substituted or unsubstituted aromatic group.

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Rule 1.12b
10 6. The compound of Claim 6, wherein ring A is a substituted or unsubstituted phenyl.

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Rule 1.12b
7. The compound of Claim 1, wherein R¹ is a cyclopentyl group, a hydroxycyclopentyl or an isopropyl.

9. A compound selected from the group consisting of
15 N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2-(trifluoromethoxy)-1-benzenesulfonamide;
N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-chlorophenyl)-2-chloro-1-benzenesulfonamide;
N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-chlorophenyl)-2-fluoro-1-benzenesulfonamide;
20 N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2-chloro-1-benzenesulfonamide;
N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-chlorophenyl)-3-fluoro-1-benzenesulfonamide;
25 N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-chlorophenyl)-1-benzenesulfonamide;
N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-nitrophenyl)-1-benzenesulfonamide;
N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-

- chlorophenyl)-3-(trifluoromethyl)-1-benzenesulfonamide;
N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-chlorophenyl)-4-chloro-1-benzenesulfonamide;
N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-chlorophenyl)-2-cyano-1-benzenesulfonamide;
N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2-nitro-1-benzenesulfonamide;
N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2,6-difluoro-1-benzenesulfonamide;
- 10 N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-methoxyphenyl)-1-benzenesulfonamide;
N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2,3,4-trifluoro-1-benzenesulfonamide;
N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-4-bromo-2-fluoro-1-benzenesulfonamide;
- 15 N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2,5-difluoro-1-benzenesulfonamide;
N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-3,4-difluoro-1-benzenesulfonamide;
- 20 N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2-bromo-1-benzenesulfonamide;
N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2,6-dichloro-1-benzenesulfonamide;
N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2,4,6-trichloro-1-benzenesulfonamide;
- 25 N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2,4-dichloro-1-benzenesulfonamide;
N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2-chloro-4-fluoro-1-benzenesulfonamide;

- N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2,4-difluoro-1-benzenesulfonamide;
- N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2-iodo-1-benzenesulfonamide;
- 5 N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2,3-dichloro-1-benzenesulfonamide;
- N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-4-bromo-2,5-difluoro-1-benzenesulfonamide;
- N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2-chloro-4-cyano-1-benzenesulfonamide;
- 10 N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2-chloro-6-methyl-1-benzenesulfonamide;
- N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-3-chloro-2-methyl-1-benzenesulfonamide;
- 15 N2-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-4,5-dibromo-2-thiophenesulfonamide,
- N2-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-5-bromo-2-thiophenesulfonamide,
- N2-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-3-bromo-5-chloro-2-thiophenesulfonamide,
- 20 N3-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2,5-dichloro-3-thiophenesulfonamide,
- N4-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2,1,3-benzothiadiazole-4-sulfonamide,
- 25 N4-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-2,1,3-benzoxadiazole-4-sulfonamide,
- N4-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-fluorophenyl)-7-chloro-2,1,3-benzoxadiazole-4-sulfonamide,
- N4-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-

fluorophenyl)-7-methyl-2,1,3-benzothiadiazole-4-sulfonamide,
N4-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-
fluorophenyl)-5-methyl-2,1,3-benzothiadiazole-4-sulfonamide,
N4-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-
fluorophenyl)-5-chloro-2,1,3-benzothiadiazole-4-sulfonamide,
N-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-
fluorophenyl)-(2-nitrophenyl)methanesulfonamide; and
N1-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-
fluorophenyl)-2,5-dibromo-3,6-difluoro-1-benzenesulfonamide;
and pharmaceutically acceptable salts thereof.

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15 10. The compound of Claim 1, wherein R₂ is -H.

11. The compound of Claim 1, wherein L is -O-, -NHSO₂R-, -NHC(O)O-, or -NHC(O)R-.

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12. A method of inhibiting protein kinase activity comprising administering a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof.

13. The method of Claim 12 wherein said protein kinase is selected from the group consisting of KDR, FGFR-1, PDGFR β , PDGFR α , IGF-1R, c-Met, Flt-1, TIE-2, Lck, Src, fyn, Lyn, Blk, and yes.

25 14. The method of Claim 12 wherein the activity of said protein kinase affects

15. The method of Claim 12 wherein the activity of said protein kinase affects angiogenesis, vascular permeability, immune responses or inflammation.

16. A method of treating a patient having a condition which is mediated by protein kinase activity, said method comprising the step of administering to the patient a therapeutically effective amount of a compound of Formula I as defined in Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolite thereof.
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17. The method of Claim 16 wherein said protein kinase is selected from the group consisting of KDR, Flt-1, PDGFR β , PDGFR α , IGF-1R, c-Met, TIE-2, Lck, Src, fyn, Lyn, Blk, and yes.
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18. The method of Claim 16 wherein the condition mediated by protein kinase activity is a hyperproliferative disorder.
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19. The method of Claim 16 wherein the activity of said protein kinase affects angiogenesis, vascular permeability, immune responses or inflammation.
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20. The method of Claim 16 wherein the activity of said protein kinase affects angiogenesis or vascular permeability.
21. The method of Claim 16 wherein the protein kinase is a protein serine/threonine kinase or a protein tyrosine kinase.
22. The method of Claim 16 wherein the condition mediated by protein kinase activity is one or more ulcers.
- 25

- a
23. The method of Claim 21 wherein the ulcer or ulcers are caused by a bacterial or fungal infection; or the ulcer or ulcers are Mooren ulcers; or the ulcer or ulcers are a symptom of ulcerative colitis.
- 5 24. The method of Claim 16 wherein the condition mediated by protein kinase activity is Lyme disease, sepsis or infection by Herpes simplex, Herpes Zoster, human immunodeficiency virus, parapoxvirus, protozoa or toxoplasmosis.
- 10 25. The method of Claim 16 wherein the condition mediated by protein kinase activity is von Hippel Lindau disease, pemphigoid, psoriasis, Paget's disease or polycystic kidney disease.
- 15 26. The method of Claim 16 wherein the condition mediated by protein kinase activity is fibrosis, sarcoidosis, cirrhosis, thyroiditis, hyperviscosity syndrome, Osler-Weber-Rendu disease, chronic occlusive pulmonary disease, asthma, exudates, ascites, pleural effusions, pericardial effusions, pulmonary edema, cerebral edema or edema following burns, trauma, radiation, stroke, hypoxia or ischemia.
- 20 27. The method of Claim 16 wherein the condition mediated by protein kinase activity is ovarian hyperstimulation syndrome, preeclampsia, menometrorrhagia, or endometriosis.
- 25 28. The method of Claim 16 wherein the condition mediated by protein kinase activity is chronic inflammation, systemic lupus, glomerulonephritis, synovitis, inflammatory bowel disease, Crohn's disease, glomerulonephritis, rheumatoid arthritis and osteoarthritis, multiple sclerosis or graft rejection.

29. The method of Claim 16 wherein the condition mediated by protein kinase activity is sickle cell anaemia.
30. The method of Claim 16 wherein the condition mediated by protein kinase activity is an ocular condition.
31. The method of Claim 29 wherein the ocular condition is ocular or macular edema, ocular neovascular disease, scleritis, radial keratotomy, uveitis, vitritis, myopia, optic pits, chronic retinal detachment, post-laser treatment complications, conjunctivitis, Stargardt's disease, Eales disease, retinopathy or macular degeneration.
32. The method of Claim 16 wherein the condition mediated by protein kinase activity is a cardiovascular condition.
33. The method of Claim 31 wherein the condition mediated by protein kinase activity is atherosclerosis, restenosis, ischemia/reperfusion injury, vascular occlusion, venous malformation, or carotid obstructive disease.
34. The method of Claim 16 wherein the condition mediated by protein kinase activity is cancer.
35. The method of Claim 33 wherein the cancer is a solid tumor, a sarcoma, fibrosarcoma, osteoma, melanoma, retinoblastoma, a rhabdomyosarcoma, glioblastoma, neuroblastoma, teratocarcinoma, an hematopoietic malignancy and malignant ascites.
36. The method of Claim 34 wherein the cancer is Kaposi's sarcoma, Hodgkin's disease, lymphoma, myeloma or leukemia.

37. The method of Claim 16 wherein the condition mediated by protein kinase activity is Crow-Fukase (POEMS) syndrome or a diabetic condition.
- 5 38. The method of Claim ³⁷ ~~36~~ wherein the diabetic condition is insulin-dependent diabetes mellitus, glaucoma, diabetic retinopathy or microangiopathy.
- 10 39. A method of decreasing fertility in a patient, said method comprising the step of administering to the patient an effective amount of a compound of Formula I as defined in Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolite thereof.
- 15 40. The method of Claim 16 wherein the compound of Formula I or a physiologically acceptable salt, prodrug or biologically active metabolite thereof is administered in an amount effective to promote angiogenesis or vasculogenesis.
- 20 41. The method of Claim ⁴⁰ ~~39~~ wherein the protein kinase is Tie-2.
- 25 42. The method of Claim ⁴⁰ ~~39~~ wherein the compound of Formula I, or physiologically acceptable salt, prodrug or biologically active metabolite thereof, is administered in combination with a pro-angiogenic growth factor.
- 25 43. The method of Claim ⁴² ~~41~~ wherein the pro-angiogenic growth factor is selected from the group consisting of VEGF, VEGF-B, VEGF-C, VEGF-D, VEGF-E, HGF, FGF-1, FGF-2, derivatives thereof and antiiodotypic antibodies.
- 25 44. The method of Claim ⁴⁰ ~~39~~ wherein the protein kinase-mediated condition is anemia, ischemia, infarct, transplant rejection, a wound, gangrene or necrosis.

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44.

The method of Claim 16 wherein the protein kinase activity is involved in T cell activation, B cell activation, mast cell degranulation, monocyte activation, the potentiation of an inflammatory response or a combination thereof.

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